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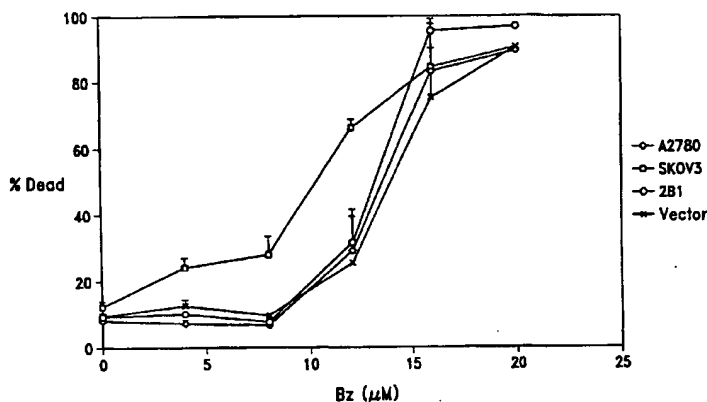
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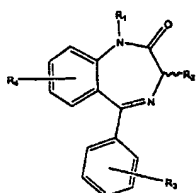
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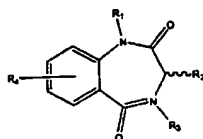
(54) Title: USE OF BENZODIAZEPINES FOR TREATING AUTOIMMUNE DISEASES INDUCED BY APOPTOSIS



Ovarian cancer cells are killed by Bz. Ovarian cancer cell lines were treated in culture media containing 2% FBS and 1% DMSO with increasing concentrations of Bz. Cell death was measured after 24 hours of treatment by flow cytometry on the basis of propidium iodide uptake. Data presented as mean value with standard deviation.



(I)



(II)

(57) Abstract: Benzodiazepine compounds, and methods for using those compounds are provided. Some of the benzodiazepine compounds include 1,4-benzodiazepine-2-one and 1,4-benzodiazepine-2,5-dione compounds of structures (I) or (II): wherein R_1 , R_2 , R_3 and R_4 are as defined. The invention also includes enantiomers, pharmaceutically acceptable salts, prodrugs or derivatives of the benzodiazepine compounds. Any one or more of these benzodiazepine compounds can be used to treat a variety of dysregulatory disorders related to cellular death. Such disorders include autoimmune disorders, inflammatory conditions, hyperproliferative conditions, viral infections, and atherosclerosis. In addition, the above compounds can be used to prepare medicaments to treat the above-described dysregulatory disorders. The benzodiazepines can also be used in drugs screening assays and other diagnostic methods.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/11599

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/5513 A61P37/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, EMBASE, CHEM ABS Data, BIOSIS, SCISEARCH, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>TANIMOTO, YUTAKA ET AL: "Benzodiazepine receptor agonists modulate thymocyte apoptosis through reduction of the mitochondrial transmembrane potential"</p> <p>JPN. J. PHARMACOL. (1999), 79(2), 177-183, XP000957572</p> <p>page 182, column 2, paragraph 3 -page 183, column 1, paragraph 1</p> <p>---</p> <p>-/--</p>	<p>1-4, 8-12, 21-26, 30-32, 61-63, 67,69, 71, 73-77, 89-95, 99-107</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

Inter. nal Application No

PCT/US 00/11599

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BLUM P ET AL: "Stiff-person syndrome: an autoimmune disease." MOVEMENT DISORDERS, (1991) 6 (1) 12-20. REF: 40, XP000957552 page 12, column 1 -column 2 ---	11,12, 24-26, 30-32, 69,75-77
X	TAUPIN V ET AL: "ENDOGENOUS ANXIOGENIC PEPTIDE ODN DIAZEPAM-BINDING INHIBITOR AND BENZODIAZEPINES ENHANCE THE PRODUCTION OF INTERLEUKIN-1 AND TUMOR NECROSIS FACTOR BY HUMAN MONOCYTES" LYMPHOKINE AND CYTOKINE RESEARCH, vol. 10, no. 1-2, 1991, pages 7-14, XP000957571 ISSN: 1056-5477 page 7, column 2, paragraph 2 page 12, column 1, paragraph 4 ---	11,12, 24-26, 30-32, 69,75-77
X	SCHLUMPF: "delayed developmental immunotoxicity of..." TOXICOL. IN VITRO, vol. 8, no. 5, 1994, pages 1061-1065, XP000957564 page 1061, column 1, paragraph 2 page 1064, column 1, paragraph 5 ---	11,12, 24-26, 30-32, 69,75-77
X	EP 0 349 949 A (FUJISAWA PHARMACEUTICAL CO) 10 January 1990 (1990-01-10) page 3, line 1 - line 5 ---	1-12, 21-32, 61-67, 69,71, 73-80, 89-107, 115,117
X	MILLER K A ET AL: "Benzodiazepines prevent neuronal death by apoptosis and necrosis in the gerbil hippocampus following transient cerebral ischemia." SOCIETY FOR NEUROSCIENCE ABSTRACTS, vol. 24, no. 1-2, 1998, page 979 XP000957679 28th Annual Meeting of the Society for Neuroscience, Part 1; Los Angeles, California, USA; November 7-12, 1998 ISSN: 0190-5295 the whole document --- -/--	1-4, 8-10, 21-23, 61-63, 67,71, 73,74, 89-92, 95, 99-106

INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>MALGRANGE: "beta-carbolines induce apoptotic cell death..." NEUROREPORT, vol. 7, no. 18, 1996, pages 3041-3045, XP000957563</p> <p>page 3043, column 1, paragraph 3 -----</p>	<p>1-4, 8-10, 21-23, 61-63, 67,71, 73,74, 89-92, 95, 99-106</p>